Alveolar Hydatid Disease of the Liver: *

Rationale and Technics of Surgical Treatment

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THIS PAPER summarizes our experience with eight cases of alveolar hydatid disease (three of which were previously reported [21]) and is especially concerned with three patients in whom we performed hemihepatectomy in an attempt to cure an otherwise fatal disease.

There are two distinct helminthic diseases caused by larval cestodes of the genus *Echinococcus*. Most of the world's literature has dealt with the more common cystic hydatid disease caused by *E. granulosus*. A second distinct clinical entity, alveolar hydatid disease, is caused by *E. multilocularis,* and differs from the cystic form in almost every respect: natural history, pathogenesis, clinical course, prognosis, and management. In man the alveolar form usually affects the liver, where it produces an invasive mass that is so intimately involved with liver parenchyma as to make impossible the development of a surgical plane of cleavage. We believe that the only rational treatment for this disease is a radical, *en bloc* resection of the part of the liver in which it is found. There is no

effective medical therapy. Untreated, the parasite slowly invades and destroys the affected organs, ultimately causing the death of the host.

The difference between the two diseases is not common knowledge in North America, since most of the information on alveolar hydatid disease is found in the German and Russian medical literature, and the disease is seldom mentioned in current texts in English. An exception is Craig and Faust's *Clinical Parasitology* (Ed. 6).[4] The alveolar disease has long been known to occur in central Europe, as well as throughout much of Siberia. In North America, the causative organism is known only from the arctic zone of northern and western Alaska, although it may possibly occur in northern Canada.[11] Compared with cystic hydatid disease, alveolar hydatid disease is rare in man, although the adult cestodes have been found commonly in canine animals in some of these regions. Up to the present time, 14 cases of alveolar hydatid disease are known from North America, including 11 autochthonous cases from Alaska. One case from Canada [8] evidently was autochthonous, while another Canadian case [16, 17] and one case from the United States [20] probably represented infections acquired in Europe. Several hundred cases have been reported from Europe and the Soviet Union.

E. multilocularis (Leuckart, 1863) is a cestode closely related to *E. granulosus* but

differing from it in morphology, life cycle, mode of larval propagation, and characteristic host response. The morphologic differences have been demonstrated by Rausch,[10] Rausch and Schiller,[13] and Vogel.[18] The adult tapeworm is a parasite chiefly of foxes, with dogs sometimes serving as an accidental definitive host. Microtine rodents (voles, lemmings, etc.) acquire the infection by the ingestion of ova disseminated in canine feces. Man may become an accidental intermediate host, acquiring the disease in the same manner as the rodents. In Alaska human infection occurs chiefly in arctic villages, where many sled dogs may be infected. In view of the small number of clinical cases known from such villages where exposure to the excrement of dogs is nearly constant, it appears that man's susceptibility to infection is low. Factors that influence establishment of the parasite in any individual are unknown.

E. granulosus (Batsch, 1786) is found in stock-raising areas throughout the world, where dogs are the usual definitive host and domestic animals are the intermediate host. In northern regions the wolf is the natural final host, and caribou and moose harbor the larvae. Infection in man produces distinct cysts that are found in the lungs and liver, and less often in other organs.

The marked dissimilarities in the clinical diseases caused by the two parasites arise from the difference in the manner of propagation of the larval forms. The larvae of E. multilocularis proliferate by means of budding outward into surrounding host tissue. Such exogenous budding has been demonstrated by Rausch and Jentoft [12] in tissue cultures. The host tissue does not respond by producing an effective limiting capsule (as it does in response to infection by E. granulosus), but host parenchyma and budding parasite are inextricably intermingled. Much like a cancer, the parasite invades and destroys the affected and adjacent organs, or spreads to distant sites,
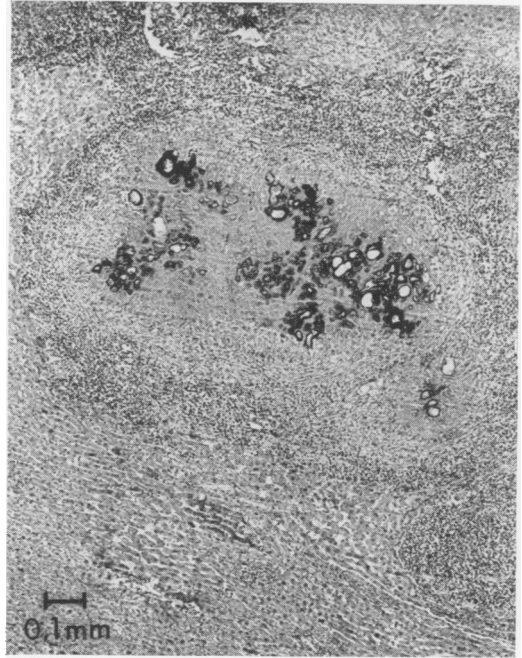

FIG. 1. E. multilocularis infection in liver (Case 7). Periodic acid-Schiff stain.

and is ultimately fatal, either because of liver failure, toxicity, or the effects of metastatic lesions.

The hepatic lesion appears grossly as a firm, yellowish-gray mass, which may replace any part of the liver, and which may present at the liver surface. Central liquefaction necrosis in advanced cases gives the mass the appearance of a large, pus-filled cavity, which has a firm wall up to several centimeters in thickness, and which may occupy half or more of the organ. Microscopically, eosinophilic laminated hyaline material, necrotic liver tissue, and fibrous tissue are found in patternless disorder. Dense scar tissue and foreign body inflammatory reaction may surround the hyaline material, which is best demonstrated when stained by the periodic acid-Schiff method.[19] These features are illustrated in Figure 1. Scolices are present only rarely.

By contrast, the larval E. granulosus grows by endogenous budding of the germinal layer within a laminated mem-

brane, and forms a distinct cyst that is surrounded by a discrete, connective tissue capsule (pericyst) of host origin. The cyst slowly enlarges and may cause symptoms by pressure. If ruptured by trauma or other cause, the liberated germinal elements may proliferate and produce multiple cysts. Often the parasite dies and persists as an inert, fluid-filled cyst that may become calcified. Only rarely, when in unusual locations such as in bones, does the larval E. granulosus bud outward and appear actively to invade the host tissue. This process, however, is quite different from the typically invasive growth of E. multilocularis.

A corollary of the difference in pathologic anatomy of the two diseases is suggested also by the results of serologic tests.* In alveolar hydatid disease, where a limiting capsule is lacking, the hemagglutination and bentonite flocculation tests are usually positive. In the cystic disease, the distinct laminated membrane and pericyst seem to form an effective barrier to passage of antigens from the parasite. In our experience, most patients with uncomplicated proven cysts have negative or weak serologic tests for echinococcosis. High titers suggest the possibility of the alveolar disease.

In both diseases the onchospheres (infective embryos) are carried in the intermediate host via portal blood from the intestines directly to the liver. Passage via lymphatics is probably less important.[9] In all our cases of infection with E. multilocularis the major disease has been in the liver, and lesions in other organs have seemed to represent secondary spread.

Surgeons throughout the world have learned to treat cystic hydatid disease more or less successfully. The cysts are amenable to such conservative technics as marsupialization, injection of formalin, evacuation of the parasite from the pericyst, and limited,

* All serologic tests were done by Dr. Irving G. Kagan, USPHS Communicable Disease Center, Atlanta, Georgia.

local resection of the cyst and immediately contiguous tissue. Such technics cannot be used in the management of alveolar hydatid disease because there is no discrete plane of cleavage between diseased and normal tissue. In order to extirpate the parasite, all of the invaded tissue and a zone of normal tissue must be resected en bloc. When the disease is in the liver, as is usual, a partial hepatectomy is necessary. We believe that this can be done most safely by lobar resection, in which control of portal and hepatic vessels is obtained initially, and the parenchyma is transected along interlobar planes according to the anatomic distribution of the vessels within the liver.

We are especially indebted to Gans,[6] whose classical treatise on hepatic surgery has elucidated the surgical implications of the intrahepatic anatomy. He emphasized that the requirements of hepatic surgery cannot ideally be met by the use of such technics as heat coagulation of the cut surface or through-and-through mattress sutures intended to maintain hemostasis at the cut curface by pressure on all the transected vessels. Reports of successful resections of large hepatic lesions, both benign and malignant, have become numerous in recent years; an increasing proportion of these is based upon an anatomic approach. Studies by Islami et al.[7] have shown the remarkable degree of hepatic regeneration that follows 70 per cent hepatectomy in dogs. These findings give confidence that massive resections of the liver can be done without causing lasting metabolic deficit.

The necessity for radical resection of the liver in cases of alveolar hydatid disease has been increasingly recognized by Soviet surgeons. Between 1912 (when V. M. Mysh performed the first known radical hepatic resection for alveolar hydatid disease) and 1959, 74 such operations were reported in the Soviet literature.[1]

Semenov,[14] who has had wide surgical experience with alveolar hydatid disease in the Soviet Union, recognized that the he-

patic lesions are not amenable to drug therapy, either systemically or by means of injections into them. He pointed out the inappropriateness of marsupialization of such lesions, since this failed to arrest the invasive growth of the parasitic tissue at the periphery of the lesion. At the time of his report in 1954, he had treated 62 persons surgically for alveolar hydatid disease of abdominal viscera. Of these, 42 were limited to simple exploratory laparotomy, with no attempt at definitive therapy; the other 20 operations included one splenectomy, two "atypical" hepatic resections, and 17 "typical" hepatic resections. The latter apparently were a modification of wedge resection of the liver, in which mattress sutures were relied on for hemostasis. There were three operative deaths among these 17 "typical" resections. The "atypical" resections consisted of progressively-enlarging, concentric excisions from the necrotic portion of the liver into the surrounding, normal tissue. Both patients so treated died, evidently from hemorrhage. On the basis of his experience, Semenov concluded that only the complete removal of alveolar hydatid lesions gave any promise of cure.

Seneque [15] reported resection of the left lobe of the liver for "multiple hydatid cysts." Although he was apparently dealing with cystic hydatid disease (*E. granulosus*), his technic was similar to that outlined by Gans [6] and by Couinaud,[2, 3] by which control of the structures in the portal hilum supplying the portion of the liver to be resected is obtained as the initial step in the procedure. However, Seneque used actual cautery for cutting the hepatic parenchyma, and electric cautery for hemostasis at the cut surface. Although his patient survived, there were significant pulmonary complications (atelectasis, pneumonia, and pleural effusion) which may have been related to the extension of the laparotomy incision

across the right diaphragm in order to gain better access to the liver.

On the basis of these reports, we were emboldened to attempt hemihepatectomy in three patients, all of whom had advanced disease, and all of whom have survived the operation and are well at present.

Our technic followed the recommendations of Gans for the most part. Our only significant innovation was the type of incision used—an inverted "Y" made by joining bilateral subcostal incisions to a vertical midline incision that split the lower sternum but neither divided the diaphragm nor entered the pleural cavities.[22] An extrapleural incision was thought to be preferable so that only the abdominal viscera would be exposed to any infective material. Overholt scapular retractors were placed beneath each costal margin, and by means of steel cables and reels attached to poles fixed at the head of the table, the overhanging portion of the rib cage was pulled cephalad. This maneuver gave excellent access to the superior surface of the liver and made management of the hepatic veins relatively easy. As a precaution, tapes were placed around the portal vein and around the inferior vena cava above and below the liver, but their use was not required. The branches of the portal vein, hepatic artery, and hepatic duct to the affected lobe were ligated and divided in the hilum as the initial step. The hepatic veins were ligated, and in some instances, in order to obtain an adequate stump, it was necessary to dissect an hepatic vein out of the liver parenchyma for a short distance. After the blood supply was thus controlled, Glisson's capsule was incised along the interlobar fissures and the parenchyma was divided bluntly with the handle of a scalpel, staying to one side of the hepatic vein that usually lay in the interlobar fissure. Vessels and ducts were divided and ligated as they were encountered, but all were of small caliber, and perfect hemostasis of the cut surface of the liver was achieved without

the use of electrocoagulation. The moderate bleeding that did occur as the parenchyma was divided in the first operation (Case 6) was attributed to the fact that not all hepatic veins draining the excised portion, especially the branches to the caudate lobe, could be dealt with until the organ had been largely transected, despite the good access allowed by the inverted "Y" incision. With one patient, the greatest blood loss occurred when deeply-situated, short, wide, hepatic veins were torn at their junction with the inferior vena cava. Such bleeding was controlled by repairing the tears with arterial silk. It was not necessary to cross-clamp the vena cava. After completion of the resection in the first two cases, large sheets of Gelfoam ® saturated with thromboplastin solution were placed across the cut surface. In retrospect we think that the Gelfoam was unnecessary and indeed may have contributed to the postoperative fever that occurred in both these patients. It was not used in the third case, and his smoother postoperative course was attributed in part to the absence of this large foreign body.

Although the procedures were long, they were tolerated surprisingly well by the three patients. Laboratory tests showed that liver function was impaired for several weeks but returned to normal in all three.

Our eight patients all had far-advanced disease when first seen. In two of the three who had resections, the lesions encroached close to an interlobar fissure; the other had extension of the disease beyond the liver. Early in its course the disease apparently causes only slight symptoms, which are not sufficient to cause the patient to seek medical attention. Both the abdominal radiograms and the serum hemagglutination test have proved useful in diagnosis, and we hope that they will increasingly assist in detection of the disease in patients with very early lesions. Data on these patients are summarized in Table 1.

Abdominal radiograms from several of our patients showed a characteristic pattern. In the area of the liver were seen clusters of faint, *stippled* or *feathery* radiodensities, which were irregular in shape, had no orderly pattern, and were not demarcated. Such radiodensities in alveolar hydatid disease have been described by Friedrich.[5] In the operated cases the actual extent of the disease has proved to be greater than the corresponding area of calcification on x-ray. The pattern of the calcifications is quite different from that seen in films of *E. granulosus* cysts of the liver, in which the radiodensities usually have a distinctly spherical shape and more sharply demarcated margins.

The hemagglutination tests have been positive in dilutions ranging from 1 : 3,200 to 1 : 200,800, and there have been no false positives. In none of the cases was eosinophilia sufficiently marked to arouse suspicion of parasitic disease.

There is still no accurate way to determine the extent of the alveolar lesions preoperatively, especially as to whether the disease has invaded across an interlobar fissure. Even at operation, the external appearance of the liver may have little bearing on the location and extent of the disease, since the hepatic parenchyma may be replaced rather than displaced by the slowly expanding lesion, and only little distortion of the organ may ensue. Palpation of the liver may give additional evidence as to the extent of involvement. Operative cholangiograms were done in two cases. In Case 6 this study demonstrated extravasation of the contrast medium into the necrotic cavity, and more importantly, revealed impingement of the diseased tissue on the right hepatic duct, lending a sense of urgency to proceeding with hepatic resection.

Because of the prolonged course this disease may take, evaluation of the results of radical resections in the treatment of alveolar hydatid disease should be de-

TABLE 1. *Summary of Data on Eight Cases of Alveolar Hydatid Disease from Alaska*

Patient	Age, Sex	Village	Location of Lesion	Serological Reactions		Treatment	Result
				Hemagglu-tination Test	Bentonite Flocculation Test		
1	57 M	Point Hope	Right lobe of liver; brain stem	1:6,400	1:320	Marsupialization	Continued drainage from hepatic sinus till death. Death due to coma from lesion in brain stem. "Grapefruit" sized lesion in liver at time of death.
2	62 F	Kotzebue	Left & right lobes of liver	1:64,000	1:20	Marsupialization	Continued drainage from sinus of liver till death. Death due to liver failure.
3	74 M	Point Hope	Right lobe of liver; left lower lobe of lung	Not done	Not done	No definitive therapy attempted	Death due to hemorrhage from acute gastric ulcer.
4	54 F	Savoonga	Right lobe of liver; retroperitoneal space	1:3,200	1:10	No definitive therapy attempted	Continued in apparent good health, but RUQ pain persisted.
5	58 F	Gambell	Left lobe of liver (1947); implant in abdominal scar (1959)	1:200	1:5	Wedge resection of hepatic lesion, 1947; excision of lesion in abdominal scar, 1959	Recovered; living, with persistent abdominal pain, 16 years after initial operation.
6	22 F	Kotzebue	Left half of liver	1:6,400	1:320	Left hemihepatectomy (60% of liver; gallbladder)	Recovered; hospitalized for 5 months after surgery. Well after 27 months.
7	46 F	Point Hope	Right half of liver	1:200,800	Not done pre-op.; 1:160 post-op.	Right hemihepatectomy (60% of liver; gallbladder)	Recovered; 70 days hospitalization. Well after 24 months.
8	12 M	Nome	Right lobe of liver; growth into diaphragm & abdominal wall (forming sinus)	1:3,200	1:5	Right hemihepatectomy (60% of liver; gallbladder)	Recovered; 143 days hospitalization. Well after 12 months.

ferred until the patients have been followed for several years.

Case Reports

The first three cases illustrate the malignant potential of alveolar hydatid disease. All three had advanced hepatic lesions, with liquefaction necrosis; one had metastases to the lung; and one had a metastasis to the brain stem. The presenting complaint in all was obstructive jaundice. In the first three cases of our series the diagnosis of hydatid disease was not made preoperatively. In none of these, however, could resection have been done, because the advanced stage of the liver lesion made them nonresectable. Marsupialization of the cavity in the liver in two patients failed notably to arrest the progression of the hepatic disease. If lasting palliation is to be achieved in a patient who has a resectable hepatic lesion, we believe that partial hepatectomy should be done. The mere presence of asymptomatic lesions elsewhere in the body does not necessarily contraindicate such palliation, since in our cases it was usually the hepatic lesion that proved lethal. Case 1 is the lone exception in our series, a metastatic echinococcus lesion in the brain being the cause of death.
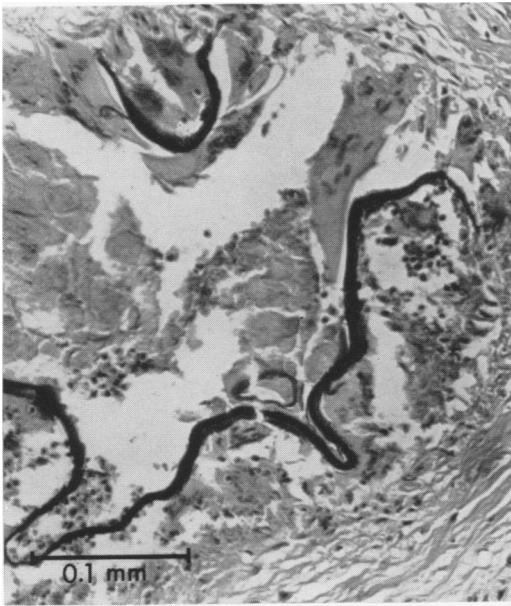
FIG. 2. Metastatic focus of *E. multilocularis* infection in the lung (Case 3). Periodic acid-Schiff stain.

Case 1. A 57-year-old Eskimo man from Point Hope, Alaska, was explored for hepatomegaly and obstructive jaundice. Initial evaluation of a liver biopsy was suggestive of tuberculosis and the subsequent demonstration of *Mycobacterium tuberculosis* in sputum culture seemed to support this diagnosis. Reappraisal of the biopsy in the light of a highly positive hemagglutination test for echinococcosis resulted in a change in diagnosis to hydatid disease of the liver. A staged marsupialization of the lesion was done at the USPHS Hospital, Seattle, that established drainage from the large central area of liquefaction necrosis. This continued to drain until the patient died a few months later. Death was due to central nervous system involvement, with terminal coma and bronchopneumonia. Autopsy revealed a *grapefruit sized* lesion in the right lobe of the liver and a lesion of the brain stem, both with the characteristic histopathologic features of alveolar hydatid disease.

Case 2. A 62-year-old Eskimo woman from Kotzebue, Alaska, underwent exploratory laparotomy because of hepatomegaly and obstructive jaundice. Biopsy of the hepatic lesion, plus strongly positive serologic tests for hydatid disease, yielded the correct diagnosis. Removal of a calculous gallbladder resulted in drainage of a large contiguous area of liquefaction necrosis in the liver, where a huge cavity completely replaced the left lobe and extended into the right lobe as well. In order to improve drainage, it was marsupialized. It continued to drain for several months until her death, often discharging large pieces of sequestrated liver. She died in her village, apparently from liver failure, and no autopsy was performed.

Case 3. This 74-year-old Eskimo man from Point Hope, Alaska, suffered a myocardial infarction while being prepared for exploration because of obstructive jaundice. However, a massive hematemesis forced an emergency laparotomy. The source of bleeding was not recognized at operation. There was a large, hard, white, irregular lesion presenting on the undersurface of the right lobe of the liver, and this was diagnosed grossly as carcinoma of the gallbladder with extension into the liver. In view of this finding, his situation was considered hopeless, but nevertheless, the duodenum was anastomosed to a bile-containing cavity in the liver, to create a biliary bypass. A few hours after the laparotomy the patient died of continuing upper gastro-intestinal hemorrhage. Autopsy revealed that the lesion of the liver had a large central area of liquefaction necrosis and was grossly typical of infection by *E. multilocularis*. A nodule was found in the lower lobe of the left lung. Both the hepatic and pulmonary lesions had the histopathologic characteristics of alveolar hydatid disease (Fig. 2). A large acute gastric ulcer was found to have been the source of hemorrhage and was the immediate cause of death. The brain was not examined.

The next two cases illustrate the indolent course of the untreated disease, before it reaches the advanced stage seen in the first three cases. Both patients are living with lesions that have extended beyond the liver, the primary site of disease in each. Both have been relatively free of symptoms and disability, and Patient 5 has lived 16 years since a lesion in her liver was first biopsied. This indolent course, coupled with the probably low rate of infection in relation to exposure, leads one to suspect that the human host has a high degree of resistance to infection by this parasite.

Case 4. A 53-year-old Eskimo woman from Savoonga, a village on St. Lawrence Island, was explored because of abdominal pain and x-ray findings that suggested cholelithiasis and alveolar

hydatid disease of the liver. No calculi were found in the gallbladder and it was not removed. A large retroperitoneal mass behind the right lobe of the liver was biopsied and presented the typical microscopic features of alveolar hydatid disease. No hepatic mass was identified at surgery, but review of the x-rays afterward indicated that there was, in fact, also a lesion within the right lobe of the liver. Serological tests for echinococcosis were strongly positive. Her convalescence was uncomplicated, and four months later she was reported to be well, although she continued to have right upper abdominal pain as before surgery.

Case 5. This 58-year-old Eskimo woman was from Gambell, the other village on St. Lawrence Island. In 1947, a lesion had been removed from the left lobe of her liver by wedge resection and had been considered grossly consistent with hydatid disease. Microscopic sections are lacking, since the specimen was apparently lost in the mail. In the summer of 1959, a painful nodule in the laparotomy scar was excised at the PHS Alaska Native Hospital in Kotzebue. The histopathologic appearance of this lesion was typical of alveolar hydatid disease (Fig. 3), showing multiple, small, cystic spaces lined by laminated hyaline membrane. While en route home she developed acute cholecystitis for which she was referred to the PHS Alaska Native Hospital in Anchorage. A calculous gallbladder was removed. A dense, white, irregular, scarred area on the anterior surface of the left lobe of the liver was noted. In the opinion of the surgeon, this represented surgical scarring in the liver, but this was not confirmed by biopsy, and serologic tests were not done at that time. In June, 1960, the medical officer who saw her in the course of a routine field trip to her village found her complaining of dull, epigastric pain, and noted that her liver was enlarged and nodular. She was re-hospitalized. The hemagglutination test was positive 1 : 200, and the bentonite test was positive 1 : 5, both of which were considered to be equivocal for diagnosis. However, x-ray disclosed typical calcifications in both lobes of her liver. An intradermal test with *Echinococcus* antigen was positive. In view of the typical calcifications in both lobes of the liver, hepatomegaly, and serologic tests for echinococcosis, she was believed still to have alveolar hydatid disease. Because of the previously proved extension of the disease into the abdominal wall and the probability that both lobes of her liver were affected, resection was not attempted. She returned to her village where she is still living, 16 years after the original biopsy.
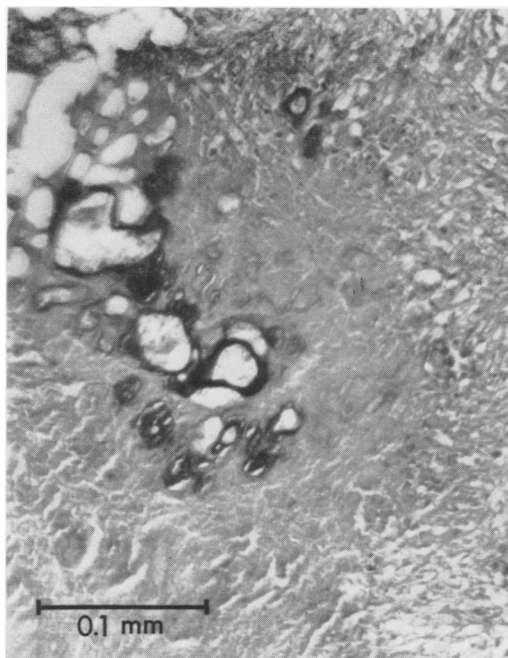

FIG. 3. *E. multilocularis* infection recurrent in laparotomy scar. Primary site in liver (Case 5). Periodic acid-Schiff stain.

The last three cases are those who underwent hemihepatectomy. All had advanced lesions; two had disease that was confined to one lobe (one right, one left) but situated very close to the interlobar fissure that was the line of resection in each. Case 6 is unusual in that the patient had marked systemic symptoms and impaired liver function despite a resectable lesion. On the other hand, Case 7 had mild and nonspecific symptoms, despite a large lesion with central necrosis that occupied most of her right lobe. Likewise, the last patient (Case 8) had only minimal symptoms, despite having two separate areas of disease in the liver, each of which had invaded adjacent structures. His first symptom was slight tenderness in a "cold" abscess that was related to a sinus from his liver. The lack of local inflammation in proportion to the extent of invasion is reminiscent of the course of extrapulmonary tuberculosis.
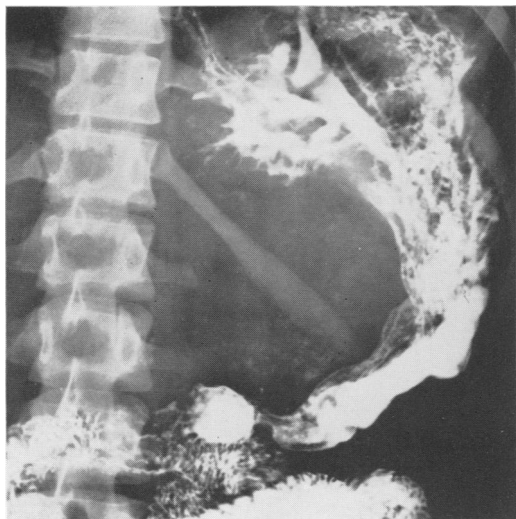
FIG. 4. Radiograph showing displacement of stomach to the left by the greatly enlarged left lobe of the liver (Case 6).

Case 6. This 22-year-old Eskimo woman from Kotzebue, Alaska, was admitted to the hospital there January 25, 1960, with a history of generalized pruritus of a week's duration. On examination she was found to have widely disseminated, cutaneous excoriations from scratching. Jaundice, hepatomegaly, and a stony-hard mass in the epigastrium, which was believed to be connected with the liver were also noted. A presumptive diagnosis of *E. multilocularis* infection of the

FIG. 5. Cholangiogram showing filling of necrotic cavity in the left lobe by radio-opaque material and narrowing of right hepatic duct (Case 6).

liver was made, and she was transferred to the PHS Alaska Native Hospital in Anchorage.

Laboratory studies revealed: hemagglutination test for echinococcosis positive in dilution of 1 : 6,400; bentonite flocculation test positive in a dilution of 1 : 320; hemoglobin 10.7 Gm.%; hematocrit 35%; WBC 8,550. The maximum eosinophilia noted at any time was 3.0%. Serum bilirubin was 6.5 mg.%, serum albumin 2.5 mg.%, serum globulin 3.5 mg.%, cephalin flocculation 4+ in 48 hours, alkaline phosphatase 16.2 Bodansky units, and prothrombin time 100% of normal. Upper gastro-intestinal series showed displacement of the stomach by an enlarged left lobe of the liver (Fig. 4). Faint calcific stippling in a pattern characteristic of alveolar hydatid lesions may also be noted in the left lobe of the liver in this figure.

Exploration of the abdomen was done on February 2, 1960. The entire liver was markedly enlarged. Except for its size the right lobe appeared relatively normal, whereas the left lobe had the gross characteristics of far-advanced infection by *E. multilocularis*. The liver was biopsied, a T-tube was placed in the common bile duct, and definitive resection was not undertaken.

Postoperative T-tube cholangiograms showed extravasation of contrast medium into a large cavity in the left lobe of the liver, which was the probable source of particulate matter that appeared in the T-tube from time to time. More importantly, the cholangiogram demonstrated narrowing of the right hepatic duct, believed due to the encroachment of the echinococcal lesion (Fig. 5). It appeared that only a little more progression of the disease would result in total obstruction of the right hepatic duct at its confluence with the left hepatic duct, thus making surgery infinitely more difficult. It was believed, however, that surgery offered the only hope of eradicating a progressive process which we considered already very nearly beyond a treatable stage. Therefore, on March 9, 1960, a left hemihepatectomy was done, using the technic described above. Dissection of the portal hilum was made tedious by scarring from previous surgery. The disease in the left lobe was so far advanced that freeing this structure from the diaphragm resulted in entering the necrotic cavity in the left lobe with the release of about 1,700 ml. of yellow, turbid fluid containing much particulate matter. The left half of the liver was removed, including the left lobe, the quadrate and caudate lobes, the gallbladder, and a small margin of liver just to the right of the gallbladder fossa. Figure 6 illustrates the remaining liver and hilar structures at the end of the resection. It is believed that some parasitic tissue was left, af-

fixed to and surrounding the right portal vein. Bleeding from the liver parenchyma was more than was anticipated, but the cut curface was perfectly dry at the end of the resection. Vigorous bleeding also occurred from a laceration of the vena cava, but was controlled by suturing. The immediate postoperative course was uneventful. Late in her convalescence, she had intermittent drainage from a drain site, but exploration failed to reveal the suspected abscess. Subsequently the sinus healed. She gradually regained weight from a postoperative low of 94 pounds to her preoperative weight of 120 pounds. By mid-July her BSP retention was only 5.0% in 45 minutes. She is now asymptomatic (May, 1962) and the hemagglutination test titer has dropped from 1 : 6,400 to 1 : 1,600. She weighs 142 pounds.

There would be greater assurance of cure of this patient, if the resection could have been carried out earlier, before the disease had extended to the right portal vein.

Case 7. This 46-year-old Eskimo woman from Point Hope, Alaska, had been examined by a USPHS medical officer on a field trip in her village because of her complaints of backache, occasional slight pain in the right upper abdomen, and a weight loss of ten pounds. She was found to have hepatomegaly, and a radiogram revealed stippled calcifications in the right lobe of the liver, typical of infection by *E. multilocularis* (Fig. 7). The hemagglutination test for echinococcosis was positive in a dilution of 1 : 200,800 (the highest titer we had encountered), but she was found to have no eosinophilia, no evidence of obstructive jaundice, and no significant impairment of liver function with the exceptions of elevation of the serum globulin to 4.0 Gm.% and BSP retention of 7.0% in 45 minutes. Chest x-ray and upper gastro-intestinal series were normal.

At operation on May 11, 1960, the right lobe of the liver was found to be markedly enlarged, extending four fingers' breadth below the right costal margin. Along the right lateral aspect of the liver there was palpable a hard, yellowish, irregular lesion, which cut with the consistency of cartilage, and the surface of which exhibited an alveolar pattern. Palpation indicated that the induration extended to about the midline of the liver, suggesting that the disease was limited to the anatomical right lobe of the liver. An operative cholangiogram showed dilation of the common bile duct but no major distortion of the intrahepatic bile ducts (Fig. 8). No extravasation of contrast medium into the lesion was seen, in contrast to the findings in Case 6. Frozen-section biopsy was consistent with *E. multilocularis* infection of the liver.
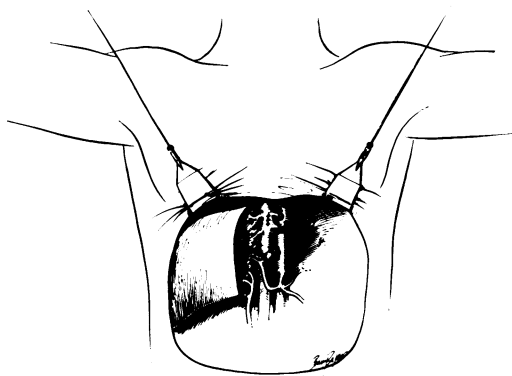

FIG. 6. Line drawing showing status of the abdomen after hepatic resection (Case 6).

A right hemihepatectomy was carried out, the specimen including about 60% of the total liver mass, together with the gallbladder. The liver was densely adherent to the right diaphragm and to the parietes posteriorly and toward the right, but no fluid was spilled from the lesion in the course of its removal, and the plane of transection in the liver did not pass through any portion of the parasitic tissue. The specimen weighed 1.7 Kg. There were no significant postoperative complications. Beginning a week postoperatively there was a transient fever and a small right pleural effusion, which cleared promptly. On the day after surgery the hematocrit was 42%, SGOT 90 units, and SGPT 140 units. On the sixth day BSP retention was 11% in 45 minutes and was 4.0% within three weeks.
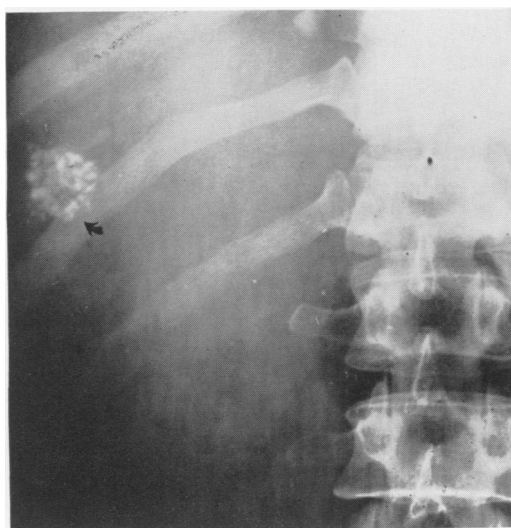

FIG. 7. Radiograph showing stippled calcification typical of *E. multilocularis* infection of the liver (Case 7).
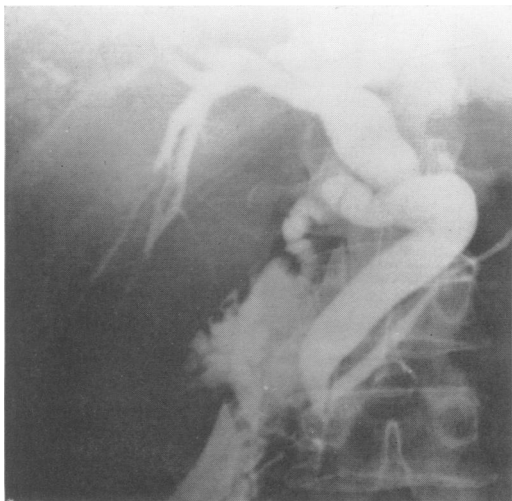
FIG. 8. Cholangiogram showing dilated common bile duct (Case 7).

Histopathologic examination of the lesion revealed a granulomatous, inflammatory process with severe necrosis. Grossly, large areas of central liquefaction were noted (Fig. 9). These changes are typical of alveolar hydatid disease of the liver.

Two years later the patient is reported to be clinically well, and her hemagglutination test titer had dropped to 1 : 1,600 by February, 1962.

Case 8. This 12-year-old Eskimo boy from Nome had spent his first six years in Wales, Alaska. In November, 1960, Dr. John A. Barrow, III, examined him because of tenderness over the right lower chest, and drained a "cold" abscess through a subcostal incision. When the ensuing

sinus failed to heal and all studies failed to show tuberculosis, he was transferred to the PHS Alaska Native Hospitals, first at Kotzebue, and later at Anchorage. Injection of the sinus showed a cavity in the abdominal wall at the tip of the ninth rib. Adjacent to this were feathery calcifications within the liver like those described above, but in two separate clusters. Biopsy of the wall of the sinus showed one band of laminated hyaline material surrounded by foreign body inflammatory reaction. The hemagglutination test was positive in dilution 1 : 3,200, and the bentonite flocculation test in dilution 1 : 5. Eosinophilia ranged from 1.0 to 5.0%. All liver function tests were normal.

At operation on June 5, 1961, the patient was found to have two separate areas of disease, both in the right lobe of the liver. One was in continuity with the sinus through the abdominal wall, and the other extended into the diaphragm where it formed a nodular mass covered by intact parietal pleura (Fig. 10). The right lobe, quadrate lobe, and gallbladder were resected *en bloc* with a core of abdominal wall surrounding the sinus and with a comparable core of diaphragm. Otherwise the hepatic resection followed the technic described above. Gelfoam ® was not used to cover the cut surface of the liver, which was completely dry. The defects in the abdominal wall and diaphragm were repaired without difficulty. Microscopic sections showed the typical pattern of alveolar hydatid disease. There were no significant postoperative complications. Within 16 days postoperatively his serum SGOT, SGPT, bilirubin, proteins, prothrombin time, alkaline phosphatase, bromsulfalein excretion, and thymol turbidity tests had all returned to normal. Sedimentation rate and body temperature, however, remained slightly elevated for several weeks. His serologic
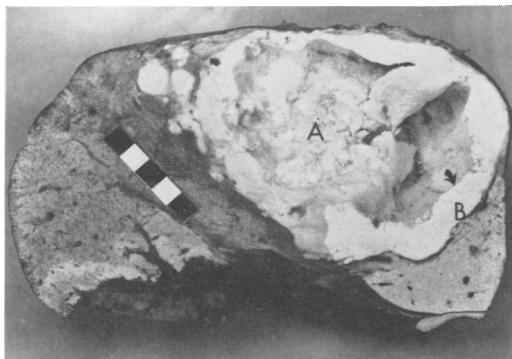

FIG. 9. Resected right lobe of liver showing central cavity (A) that contained liquefied, necrotic debris. The thick wall (B) of the cavity is hepatic tissue infiltrated by *E. multilocularis* (Case 7). Each space of scale has value of 1.0 cm.
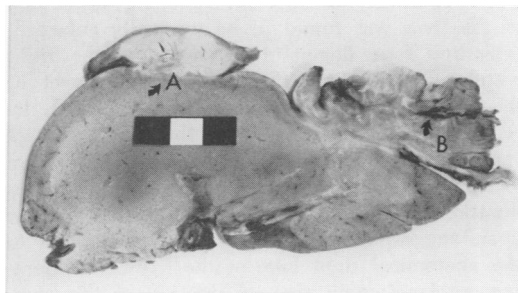

FIG. 10. Sagittal section of resected right lobe of liver showing invasion of diaphragm and abdominal wall (arrows). "A" indicates the diaphragm and parietal pleura; "B" indicates the sinus extending from the diseased liver through the abdominal wall (Case 8). Each space on scale has value of 1.0 cm.

tests for echinococcosis have both become negative (March, 1962), and a year after operation he is clinically well.

Summary

Cestodes of the genus *Echinococcus* cause two distinct diseases: the well-known cystic hydatid disease found in stock-raising areas, caused by *E. granulosus*, and the more rare alveolar hydatid disease, which is limited to the northern hemisphere and is caused by the biologically and morphologically distinct *E. multilocularis*.

Eight cases of alveolar hydatid disease of the liver are reported from Alaska, including three patients who underwent hemihepatectomy for advanced lesions. Radical resection is concluded to be the only rational treatment for this otherwise progressive and fatal disease.

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